

## A. Destexhe

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## Is the Purpose of Reverse Spike-Frequency Adaptation to Enhance Correlations? Focus on “A Model of Reverse Spike Frequency Adaptation and Repetitive Firing of Subthalamic Nucleus Neurons”

### A. Destexhe

*Integrative and Computational Neuroscience Unit (UNIC), Centre National de la Recherche Scientifique, 91198 Gif-sur-Yvette, France*

Central neurons have the capacity of encoding stimulus by producing repetitive firing, with a firing frequency proportional to stimulus amplitude. This property is measured experimentally by computing the frequency-current (f-I) relation, which is linear in most cases (e.g., Connors and Gutnick, 1990). In some neurons, however, more complex f-I relations are observed. It is known since about 40 years (Granit et al., 1963) that motoneurons have a sigmoidal f-I relation, which defines “primary” and “secondary” ranges of firing. In the secondary range of firing, the steep slope of the f-I relation provides an enhanced response gain for inputs within this range. Besides this gain change, however, no clear functional role has been shown to be associated with such nonlinear f-I relations.

The interest of the secondary range of firing may reside in another property associated to it. Many neurons respond to constant current stimuli by producing trains of action potentials with progressively longer interspike intervals. This “spike-frequency adaptation” is a very commonly observed property of central neurons and is prominent in neocortical neurons for example (McCormick et al., 1985). However, neurons of subthalamic nuclei (which are a part of the basal ganglia—thalamus—cortex loop), can show opposite adaptation properties according to input range: they show conventional spike-frequency adaptation in the primary range of firing, but they produce trains that increase in frequency in the secondary range of firing (Hallworth et al., 2003). This “reverse spike-frequency adaptation” is a property relatively rarely seen (see Domich et al., 1986 for thalamic neurons), but here again, no clear functional role has been attributed to this property.

The beginning of an answer may have been provided in a series of recent papers on subthalamic neurons. The authors first investigated the ionic bases of the above properties using in vitro electrophysiology (Hallworth et al., 2003). They showed that the secondary range of firing, as well as the reverse adaptation, are both sensitive to high-threshold  $\text{Ca}^{2+}$  channels, and are strongly affected by drugs that affect calcium-dependent  $\text{K}^+$  currents. In the this issue (p. 1963–1980), Wilson and coauthors go one step further by offering a comprehensive computational study of these phenomena (Wilson et al. 2004).

Using both simple integrate-and-fire models with spike-triggered conductances, and biophysical (Hodgkin-Huxley type) models, the authors analyze the details of the mechanisms underlying the repetitive firing of subthalamic neurons. They take advantage of the possibility of obtaining mathematical expressions of the firing frequency in simple models, and

test these predictions using the more complex biophysical models. The main findings are that a combination of fast and slow spike-triggered  $\text{K}^+$  conductances (responsible for after-hyperpolarizations or AHP) can produce nonlinear f-I relations similar to experiments. Using an additional spike-triggered inward current, producing an after-depolarization (ADP), produces the reverse spike-frequency adaptation in the secondary firing range. The pharmacological experiments altering high-threshold  $\text{Ca}^{2+}$  currents and  $\text{Ca}^{2+}$ -activated  $\text{K}^+$  currents can be explained by this model. Interestingly, the model shows that the existence of a secondary range does not imply reverse adaptation, although both occur for the same input range.

Assuming that these mechanisms are correct, one still needs to explain what functional relevance they may have. Here again, the present article provides an important hint. The secondary range of firing is also seen—although less prominently—with more realistic paradigms consisting of conductance-based synaptic inputs instead of injected currents. When submitted to Poisson-distributed random inputs, the model exhibits correlations between successive interspike intervals. This observation is interesting because it shows that reverse spike-frequency adaptation can lead to production of correlations. In contrast, the conventional spike-frequency adaptation is thought to play the opposite role: it was proposed (Barlow, 1961) that adapting processes are necessary to reduce the redundancy of inputs by decorrelating them, therefore performing a form of novelty detection. Indeed, models (e.g., Wang et al., 2003) have shown that the conductances responsible for spike-frequency adaptation can provide an efficient mechanism to perform such a decorrelation. This decorrelation can also be performed through anti-Hebbian synaptic plasticity (Barlow and Foldiak, 1989; Roberts and Bell, 2000) or with short-term synaptic depression (Goldman et al., 2002). On the other hand, the more classic Hebbian plasticity would lead to reinforcing pre-existing correlations, similar to reverse spike-frequency adaptation.

Perhaps the most interesting property of subthalamic neurons is that they can play both roles. Because they can show both adaptation and reverse adaptation, these neurons could act either as “decorrelators” or as “correlators”, depending on the level of activity. This dual function cannot be realized using synaptic plasticity because the type of plasticity at synapses (Hebbian vs. anti-Hebbian) is fixed in most cases. Thus, subthalamic networks could function according to two fundamentally different modes: a “search mode” for low activity levels, where adaptation dominates and tend to extract novel features, and a “convergence mode” for higher activity levels, where reverse adaptation tends to enhance correlations. Obviously,

Address reprint requests and other correspondence to A. Destexhe (E-mail: Destexhe@iaf.cnrs-gif.fr).

other brain areas could benefit from such a duality, and indeed different activity states, “up” and “down” states in cortex or basal ganglia for example, could play this role. In any case, this is a very nice example where intrinsic neuronal conductances may have a functional impact at the network level, and it is to be hoped that the present study on subthalamic neurons will motivate similar studies in other brain regions.

## REFERENCES

- Barlow HB.** Possible principles underlying the transformations of sensory messages. In: *Sensory Communications* (Edited by Rosenblith WA), MIT Press, Cambridge, MA, 1961, pp. 217–234.
- Barlow HB and Foldiak P.** Adaptation and decorrelation in the cortex. In: *The Computing Neuron* (Edited by Durbin R, Miall C and Mitchison G.), Addison-Wesley, New York, 1989, pp. 454–472.
- Connors BW and Gutnick MJ.** Intrinsic firing patterns of diverse neocortical neurons. *Trends Neurosci.* 13: 99–104, 1990.
- Domich L, Oakson G, and Steriade M.** Thalamic burst patterns in the naturally sleeping cat: a comparison between cortically projecting and reticularis neurones. *J Physiol* 379: 429–449, 1986.
- Goldman MS, Maldonado P, and Abbott LF.** Redundancy reduction and sustained firing with stochastic depressing synapses. *J Neurosci* 22: 584–591, 2002.
- Granit R, Kernell D, and Shortess GK.** Quantitative aspects of repetitive firing of mammalian motoneurons caused by injected currents. *J Physiol* 168: 911–931, 1963.
- Hallworth NE, Wilson CJ, and Bevan MD.** Apamin-sensitive small conductance calcium-activated potassium channels, through their selective coupling to voltage-gated calcium channels, are critical determinants of the precision, pace, and pattern of action potential generation in rat subthalamic nucleus neurons in vitro. *J Neurosci* 20: 7525–7542, 2003.
- McCormick DA, Connors BW, Lighthall JW, and Prince DA.** Comparative electrophysiology of pyramidal and sparsely spiny stellate neurons of the neocortex. *J Neurophysiol* 54: 782–806, 1985.
- Roberts PD and Bell CC.** Computational consequences of temporally asymmetric learning rules: II. Sensory image cancellation. *J Comput Neurosci* 9: 67–83, 2000.
- Wilson CJ, Weyrick A, Terman D, Hallworth NE, and Bevan MD.** A model of reverse spike frequency adaptation and repetitive firing of subthalamic nucleus neurons. *J Neurophysiol* 91: 1963–1980, 2004.
- Wang XJ, Liu Y, Sanchez-Vives MV, and McCormick DA.** Adaptation and temporal decorrelation by single neurons in the primary visual cortex. *J Neurophysiol* 89: 3279–3293, 2003.